American Journal of Medical Genetics 64:82 (1996)

Letter to the Editor

Refined Localization of the Prieto-Syndrome Locus

To the Editor:

PRS designates the locus for a syndromal form of X-linked mental retardation (Prieto syndrome) characterized by minor facial anomalies, ear malformation, abnormal growth of teeth, clinodactyly, sacral dimple, patellar luxation, malformation of lower limbs, abnormalities of the fundus of the eye, and subcortical cerebral atrophy [Prieto et al., 1987]. Linkage analysis localized the disease locus between DXS84 (Xp21.1) and DXS255 [Xp11.22; Watty et al., 1991]. Here we present additional linkage data that provide further support and refinement of this localization. Individual III-18 gave birth to a male (IV-1 in Fig. 1), currently aged 2$^{7}/_{12}$ years, who clearly shows delayed psychomotor development. He began to walk at 23 months and his speech is delayed. In addition, he shows the characteristic facial anomalies, "dysplastic" ears, sacral dimple, and clinodactyly, as do all other affected males in this family.

For the linkage analysis, the inclusion of IV-1 results in 3 additional informative meioses. Furthermore, 4 additional markers were typed in this family: DXS1068 [Gyapay et al., 1994], DXS7 [Moore et al., 1992], MAO-A [Hendriks et al., 1992], and SYN/ARAF1 [Kirchgessner et al., 1991]. Data of the extended linkage study using the markers known to be linked to PRS confirm the former localization with a maximum multipoint LOD score of 3.58 in the middle of the OTC-MAO-A interval. As IV-1 inherited the OTC-allele of his maternal grandfather, and II-1 inherited the disease-associated haplotype for SYN/ARAF and MAO-A, these findings allow a refined localization of the PRS between OTC and MAO-A, reducing the localisation to a 9 cM interval [Fain et al., 1995].

Further studies with markers mapped in the interval OTC-MAOA may lead to a more precise localization of the disease locus, which would be an important step towards the identification of the gene/s involved in the disease. In any case, the present refined localisation supposes a great improvement in accuracy for future prenatal diagnoses.

Received for publication August 14, 1995; revision received December 6, 1995.

Address reprint requests to Dr. Félix Prieto, Unidad de Genética, Hospital La Fe, Avenida Campanar 21, 46009 Valencia, Spain.

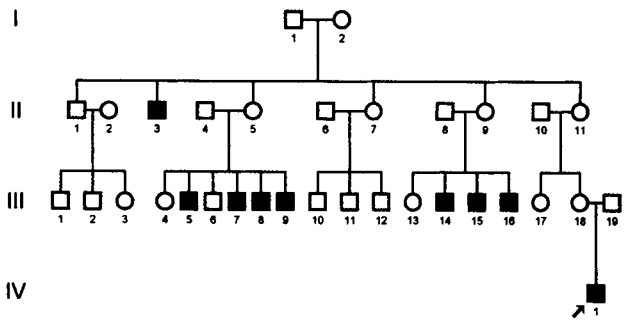

Fig. 1. Family pedigree.

REFERENCES

Fain PR, Kort EN, Chance PF, Nguyen K, Reed DF, Econs MJ, Barker DF (1995): A 2D crossover-based map of the human X chromosome as a model for map integration. Nature Genet 9:261–266.

Gyapay G, Morissette J, Vignal A, Dib C, Fizames C, Millaseau P, Marc S, Bernardi G, Lathrop M, Weissenbach J (1994): The 1993–1994 Généthon human genetic linkage map. Nature Genet 7:246–339.

Hendriks RW, Chen Z-Y, Hinds H, Schuurman RKB, Craig IW (1992): An X chromosome inactivation assay based on differential methylation of a CpG island coupled to a VNTR polymorphism at the 5′ end of the monoamine oxidase A gene. Hum Molec Genet 1(3):187–194.

Kirchgessner CU, Trofatter JA, Mahtani MM, Willard HF, De Gennaro LJ (1991): A highly polymorphic dinucleotide repeat on the proximal short arm of the human X chromosome: linkage mapping of the Synapsin I/A-raf-I genes. Am J Hum Genet 49:184–191.

Moore B, Kwan S-P, Bech-Hansen NT (1992): A polymorphic dinucleotide repeat at the DXS7 locus. Nucleic Acid Res 20:929.

Prieto F, Badía L, Mulas F, Monford A, Mora F (1987): X-linked dysmorphic syndrome with mental retardation. Clin Genet 32:326–334.

Watty A, Prieto F, Beneyto M, Neugebauer M, Gal A (1991): Gene localization in a family with X-linked syndromal mental retardation (Prieto syndrome). Am J Med Genet 38:234–239.

F. Martínez
F. Prieto
Unidad de Genética
Hospital La Fe
Av. Campanar
Valencia, Spain

A. Gal
Institut für Humangenetik
Universitäts-Krankenhaus Eppendorf
Hamburg, Germany